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Genetic Basis of Alzheimer's Disease: Bangladesh Perspective

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Alzheimer's disease (AD) is the leading cause of dementia and one of the major medical challenges of our century. It is a neurodegenerative condition characterized by amyloid peptide (A) deposits and neurofibrillary tangles in the brain. It is a neurological ailment that is progressive and devastating. It is accounting for up to 80.0% of all dementia diagnoses globally[1]. In total, 40 million individuals are expected to suffer from dementia throughout the world, with this figure expected to double every 20 years until about 2050 reaching 115 million[2]. Two subtypes of Alzheimer's disease can be separated based on the age at which the illness manifests which are late-onset AD (LOAD) and early-onset AD (EOAD). The most frequent kind of AD is LOAD, which is defined as AD that begins later than 65 years of age. EOAD is most commonly diagnosed in those under the age of 65 years, accounting for roughly 1.0% to 2.0% of all cases[3].

It has been established that there are several genes which are responsible for AD. Moreover, mutations in three genes have been discovered in autosomal dominant EOAD which are the amyloid precursor protein (APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2) genes[4]. PSEN1 has around 200 variants, the majority of which are missense mutations, but there are also minor duplications and deletions, as well as bigger deletions. PSEN1 mutation carriers had a median age of onset of 43 years, with the vast majority of cases occurring before the age of 60 years[2]. According to the AD and FTD Mutation Database, there are around 16 mutations in PSEN2 gene[5].

Genomic research is quickly advancing and it has the potential to alter many aspects of health care, including illness prevention, diagnosis, and treatment. Several genes linked to Alzheimer's disease (AD) have currently been identified[6]. The study of Alzheimer's disease's (ADs) diverse genetics has progressed faster than that of any other prevalent disease. Not only have three rare autosomal dominant mutation locations been discovered, but globally inherited susceptibility polymorphisms linked to risk and age of onset distributions for familial and sporadic Alzheimer's disease have also been verified[7]. Sporadic Alzheimer's disease has a major hereditary component as well. The apolipoprotein E gene (APOE) is linked to a significant increase in the risk of EOAD and LOAD. Alzheimer's disease (AD) has a high heredity rate, with late-onset AD having a heritability of 58.0 to 79.0% and early-onset AD having a heritability of over 90% cases[8].

Genetic connection gives a solid foundation on which to develop our knowledge of the disease's genesis. Over 50 genes have now been linked to Alzheimer's disease, suggesting that it is a multi-component illness, as evidenced by pathway studies like immunity, endocytosis, cholesterol transport, ubiquitination, amyloid- and tau processing[8]. Prior to the COVID-19 pandemic, AD was the third highest cause of mortality in the United States, trailing only heart disease and cancer as a cause of death for the elderly. Most developed nations see AD as one of the most serious economic risks. According to research, the cost of Alzheimer's disease will be 7 billion USD in 2030 in the United States alone, including careers[5]. The number of people afflicted is now larger in industrialized nations, which coincides with the proportion of elderly people.

Genetic tests are a form of screening tool used on symptomatic, asymptomatic, and healthy persons. As a procedure, genetic testing uses the definition of alterations in chromosomes, genes, or proteins. Interest in these tests is growing as a result of a variety of circumstances in both developed and developing nations. Interest in these tests is growing as a result of a variety of circumstances in both developed and developing nations. One of these variables is the likelihood of early diagnosis, which reduces morbidity

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and death. Furthermore, by altering the patient's lifestyle, negative (poor) test findings might lead to a more normal existence. This translates to decreased suffering and agony. Nonetheless, test findings do not guarantee that the individual will develop a chronic condition. These test results also raise serious concerns about genetic prejudice. Furthermore, the risk of inaccurate test findings leading to unneeded medical procedures is regarded as a significant barrier to genetic testing[2]. Advances in neurodegenerative disease genetic testing have enhanced the capacity to establish precise diagnoses, give family members with recurrence risk information, and in certain circumstances identify clinical trial eligibility.

Genetic basis of Alzheimer's disease is well established in the developed country. However, there are just a few statistics on the number of Alzheimer's patients in Bangladesh. There is no available study regarding genetics of Alzheimer's Disease Patients in our country. Even, in this country, there is no accurate epidemiological data on Alzheimer's disease. Here, awareness of Alzheimer's disease as well as detection in early stage can delay the progression of the disease. As different gene implicated in AD pathogenesis in different way, so knowing the genetic basis of these patients will guide treatment and future drug development. Children of AD having genetic risk may incorporate in follow up to identify in subclinical or early stage providing a group of cases selecting for disease modifying drugs like anti amyloid monoclonal antibody in future study.

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